REMARKS/ARGUMENTS

Claims 92-94, 96-99, 104-106 and 121-135 are pending in the present application. Support for new claims 124-143 is as follows

Claims 124-126; page 11, lines 9-10, and page 32, lines 19-20;

Claims 129-131; page 32, lines 19-20 and page 35, lines 28-30; and

Claims 130-135; page 35, lines 32-34 and page 36, lines 10-14.

Applicants note the Examiner's comment that submission of a new Abstract is required because the present Abstract is not clearly indicative of the invention to which the claims are directed and state herewith that they will present a new Abstract upon indication of allowable claims by the Examiner.

Applicants also submit herewith an Information Disclosure Statement and accompanying 1449 form listing US patents 6,268,343 and 6,458,924 and note that an application in the same patent family, USSN 10/285,079, is currently pending before the USPTO. Applicants further note that in the patent family for WO 96/29342, cited by the Examiner in the present Office Action, there is a pending application USSN 09/772,607.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. 112, FIRST PARAGRAPH

The Examiner rejected claims 92-94, 96-99, 104-106 and 121-123 under 112, first paragraph because the specification "while being enabling for the use of a pharmaceutical composition containing exendin-3 or exendin-4, fragment thereof, or any combination thereof, for the treatment of diabetes mellitus, does not reasonably provide enablement for an exendin derivative that has an amino acid sequence that differs from the amino acid sequence of exendin-3 or exendin-4 by the substitution of up to ten (claim 92) or up to six (claim 93) amino acids with any alpha amino acid residue" (page 4 of Office Action).

Applicants respectfully traverse this rejection.

First, Applicants acknowledge the Examiner's statement that claims to exendin-4 or a fragment thereof were enabled and will file a continuation application to pursue such claims.

Second, with respect to enablement of the pending claims, Applicants note that the test of enablement is whether one reasonably skilled in the art could make and use the invention from the disclosure in the application coupled with information known in the art without undue experimentation. In this regard, it is well settled that a patent application need not teach what is known in the art and that the fact that experimentation may be complex does not necessarily make it undue if the art typically engages in such experimentation. Further, the presence of inoperative embodiments within the scope of a claim does not render a claim invalid if one skilled in the art could determine which embodiments were operative or inoperative with expenditure of no more effort than is normally required in the art.

Here, the pending claims are directed to derivatives of exendin-4 analogues wherein the derivative has one lipophilic substituent attached, optionally via a spacer, to an amino acid residue of the analogue which is not the N-terminal or C-terminal amino acid residue of the analogue and wherein the amino acid sequence of the analogue differs from the amino acid sequence of exendin-4 by substitution of up to 10 (claim 92), 6 (claim 93) or 4 (claim 127) amino acids or by an addition of up to 6 amino acids at the C terminus of exendin-4 (claim 124).

The application teaches that the derivatives of the invention have a protracted profile of action relative to the unmodified parent peptide (ie to an unmodified exendin-4 analog), that one measurement of protraction can be obtained by measuring the disappearance rate of the derivatives in pigs following subcutaneous injection (see pages 47-48 of the application), and citing to US patent 5,424,286, that the exendin-4 polypeptides stimulate insulin release (page 31, line 5).

Regarding information known to the skilled artisan as of the present application's earliest priority filing date of February 27, 1998, it was known that:

1) The ability of exendin polypeptides to stimulate insulin release could be measured by in vitro or in vivo assay (see col.5 lines 20-24 of US Patent 5,424,286, cited by the Examiner in the present Office Action); and

2) exendin analogs which retained biological activity had been identifed as had specific substitutions that could be made at specific residues of exendin-4 [see, for example, pages 4-8 of AU 731732 (copy attached), which is an English language counterpart of WO 97/46584 cited on page 30, line 21 of the present application and pages 10-14, Figure 4 and Tables 1-3 of US provisional application 60/065,442 filed Nov 14, 1997 (copy attached), which is incorporated by reference at page 10 of WO 98/30231].

Thus, as of the priority filing date of the present application, it was known which residues in exendin-4 could be changed to produce exendin-4 analogs that stimulate insulin release and specific analogs had been described as had methods for identifying further analogs.

Accordingly, Applicants submit that given the teachings of the specification and the information known in the art as of the priority filing date of the present application, the question of whether one reasonably skilled in the art, based on the disclosure in the application coupled with information known in the art could make and use the presently claimed invention without undue experimentation, must be answered in the affirmative. It is Applicants' position that to do otherwise and limit applicants to the specific exendin sequences exemplified in the application would unfairly allow potential infringers to use the teachings of the application to design around such a claim.

In view of the above arguments and references presented herein, Applicants submit that pending claims 92-94, 96-99, 104-106 and 121-135 are fully enabled by the present application and withdrawal of this rejection is therefore respectfully requested.

REJECTION OF THE CLAIMS UNDER 35 U.S.C. 103 (a)

The Examiner rejected claims 92-94, 96-99, 104-106 and 121-123 under section 103 as obvious over Eng (US Patent 5,424,286) taken with WO 96/29342. Eng is cited as teaching the use of a pharmaceutical composition of exendin-4 for the treatment of diabetes and for providing a means for identifying any specific analogs of exendin-4 and WO 96/29342 as teaching the attachment of a lipophilic substituent to a parent peptide by means of a spacer and hence, as showing the attachment of a lipophilic substituent which is not a C-terminal or N-terminal residue. The Examiner concludes that one would have been motivated to apply the teachings of the WO reference to the exendins of US Patent 5,424,286 because both references teach the use of the compounds disclosed therein to treat diabetes.

Applicants respectfully traverse this rejection.

While Applicants dispute the Examiner's assertion that one would have necessarily been motivated to apply the teachings of the cited WO reference to the 286 patent, Applicants also note that the Examiner's obviousness rejection is apparently based on the dislcosure at pages 3-4 of the WO reference that the spacer attached to the N-or C-terminal amino acid of the parent peptide can be an amino acid (Glu, Asp or Lys) and hence, the lipophilic group can be attached to an amino acid other than the N-or C-terminal amino acid of the parent peptide. However, **this spacer is clearly not part of the parent peptide**. Thus, the lipophilic group in the WO reference is attached either directly to the N-or C-terminal amino acid of the parent peptide or is attached to the spacer which in turn is directly attached to the N-or C-terminal amino acid of the parent peptide.

By comparison, the amendments to claim 92 presented herein make clear that the lipophilic group, or the spacer to which the lipophilic group is attached, is attached to an amino acid residue of an exendin-4 analogue which is not the N-terminal or C-terminal amino acid residue of the analogue. **Thus, the lipophilic substituent in the pending claims is attached to an amino acid of the exendin-4 analogue (ie of the parent peptide) which is not the N-terminal or C-terminal amino acid residue of the analogue.**

Accordingly, as neither US patent 5,424,286 nor the cited WO publication, either alone or in combination, teach or suggest attaching the lipophilic subtituent to an internal

amino acid of the parent peptide, Applicants submit that the pending claims are not obvious over the cited art and withdrawal of this rejection is therefore respectfully requested.

The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Please charge any deficiencies or overpayment to Deposit Account No.14-1447.

Respectfully submitted,

Date: December 23, 2004

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